TABLE 6.—Continued

Study	Subjects	Pulmonary function measure	Outcome	Comments
Speizer et al. (1980)	8,120 children, aged 6–10, in six U.S. cities	FVC and FEV_1 as percent predicted	No effect for FEV_1 or FVC	Recent analysis of this cohort demonstrated an effect for FVC and FEV_1
Ware et al. (1984)	10,000 children, aged 6–11, in six U.S. cities	FEV_1 and FVC	FVC positively associated with smoking, FEV_1 negatively associated	FEV_1 dose–response with amount smoked by mother

function as adults, particularly if they become smoking adults. No data are currently available to establish the role, if any, of the small physiologic changes in children on the development of adult obstructive lung disease.

Pulmonary Function in Adults Exposed to Involuntary Cigarette Smoke

White and Froeb (1980) reported on 2,100 asymptomatic adults drawn from a population about to enter a physical fitness program. They demonstrated statistically significant decreases in FEV_1 and MMEF as a percent of predicted in nonsmokers exposed to tobacco smoke in the work environment compared with nonexposed workers. The decrement was comparable to that seen in smokers inhaling 1 to 10 cigarettes per day. However, the absolute magnitude of the difference in mean levels of function in the smoke-exposed and unexposed groups was quite small: 160 ml (5.5 percent) for FEV_1 and 465 ml/sec (13.5 percent) for MMEF. Carbon monoxide levels were measured in the workplace and ranged from 3.1 to 25.8 ppm. The population was self-selected, response was related to current workplace exposure and did not account for people who changed jobs, and it is unclear how the ex-smokers in the population were handled in the analysis.

Comstock et al. (1981) examined 1,724 subjects drawn from two separate studies in Washington County, Maryland. They found no statistically significant greater risk of having an FEV_1 less than 80 percent of predicted in male nonsmokers exposed to wives' cigarette smoke at home. Schilling et al. (1977) did not find an effect of passive smoking exposure in adults. Both of these studies included adults in their samples who were relatively young and generally would not have had a long-term passive exposure in adult life. This point was brought out by a recently reported large study from France. Kauffmann et al. (1983) reported on a seven-city investigation in which a total of 7,818 adults were studied. In a subsample of 1,985 nonsmoking women aged 25 to 29, in which 58 percent were exposed to smoking husbands, there was a significant difference in level of MMEF between truly nonsmoking women and women of comparable ages exposed to passive smoking. This effect did not become apparent until age 40. These changes were small, and although not adjusted for differences in body size, may suggest a possible effect of long-term exposure in adult life.

The physiologic and clinical significance of these small changes in pulmonary function in adults remains to be determined. In addition, variables such as ventilation, room size, number of rooms in the home, duration of contact with the active smoker, and number of cigarettes smoked could significantly influence total exposure and

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need to be explored more fully. Differences in these exposure variables and the characterization of exposure may explain some of the differences in these study results (Table 7).

The Effect of Passive Smoke Exposure on People With Allergies, Asthma, and COLD

There are very limited data on the effects of passive smoke exposure in patients with preexisting pulmonary disease, and the available data are conflicting. Clinical studies have suggested a relationship between respiratory symptoms in asthmatics and exposure to parental cigarette smoke, but methodologic problems complicate the interpretation of the limited available data.

O'Connell and Logan (1974) identified 37 asthmatic children who were "bothered" by parental cigarette smoke. Parents of 20 of the children stopped smoking and 18 (90 percent) of the 20 children had an improvement in symptoms. The control group consisted of 15 children (2 were not followed up) whose parents did not stop smoking. Only 4 (27 percent) of the children in the control group improved. The self-selection of those parents who quit, subjective criteria for improvement, and an unclear duration of followup limit the interpretation of this data. Gortmaker and coworkers (1982) studied two populations of children aged newborn to 17 years. They found a significant association between parental reporting of children's asthma and maternal smoking. Maternal smoking alone was associated with approximately 20 percent of all asthma. The effect persisted when age and sex of the child, allergies, and family income and education were controlled in the analysis. No control was attempted for the children's own smoking habits or for increased reporting of symptoms in children of symptomatic parents. Other population-based studies (Lebowitz and Burrows 1976; Speizer et al. 1980; Schilling et al. 1977) have not shown such results.

Dahms et al. (1981) studied 10 patients with bronchial asthma and 10 normal subjects passively exposed to smoke in an environmental chamber. Pulmonary function was measured at 15-minute intervals for 1 hour after smoke exposure. Blood carboxyhemoglobin levels were measured before and after the 1-hour exposure. Carboxyhemoglobin levels in subjects with asthma increased from 0.82 to 1.20 percent. In normal subjects the increase was from 0.62 to 1.05 percent. The increases in carboxyhemoglobin in the two study groups were not significantly different. Asthmatic subjects had a decrease in forced vital capacity (FVC), forced expiratory volume in 1 second (FEV₁),and maximum mid expiratory flow rate (MMEF) to a level significantly different from their preexposure values. The decreases in asthmatic subjects were present at 15 minutes, but worsened over the course of the hour to approximately 75 percent of

TABLE 7.—Pulmonary function in adults exposed to involuntary smoking

Study	Subjects	Pulmonary function measure	Outcome	Comments
White and Froeb (1980)	2,100 adults, San Diego, California	FVC, FEV_1, and MMF as percent predicted	Significant effect of office exposure to involuntary smoke	Potential bias in selection; assessed only current cigarette smoke exposure
Comstock et al. (1981)	1,724 adults, Washington County, Maryland	FEV_1 as percent predicted	No effect of wives' smoking on husbands' pulmonary function	Includes adults aged 20 +
Kauffmann et al. (1983)	7,818 adults, seven French cities, selected subgroups	FEV_1, FVC, and MMEF	Significant effect in wives of smoking husbands in all measures; significant only for MMEF in husbands of smoking wives	Not adjusted for height; dose–response to amount of husbands' smoking for MMEF in wives; no effect below age 40

the preexposure values. Normal subjects had no change in pulmonary function with this level of exposure. In this study, subjects were not blinded as to the exposure and were selected because of complaints about smoke sensitivity. Shephard et al. (1979), in a very similar experiment, subjected 14 asthmatic subjects to a 2-hour cigarette smoke exposure in a closed room (14.6 m^3). The carbon monoxide levels (24 ppm) were similar to those predicted in the study of Dahms and coworkers. No blood carboxyhemoglobin levels were measured. Subjects were randomized and blinded to sham (no smoke) and smoke exposure and tested on two separate occasions. Data were expressed as a percentage change from the sham exposure. No significant changes in FVC or FEV_1 were observed between sham and smoke exposure periods, although 5 of 12 subjects did report wheezing or tightness in the chest on the day of smoke exposure.

The limited existing data yield conflicting results concerning the relationship between passive smoke exposure and symptoms in patients with known pulmonary disease. Further study of this important question is warranted.

Summary and Conclusions

1. Cigarette smoke can make a significant, measurable contribution to the level of indoor air pollution at levels of smoking and ventilation that are common in the indoor environment.
2. Nonsmokers who report exposure to environmental tobacco smoke have higher levels of urinary cotinine, a metabolite of nicotine, than those who do not report such exposure.
3. Cigarette smoke in the air can produce an increase in both subjective and objective measures of eye irritation. Further, some studies suggest that high levels of involuntary smoke exposure might produce small changes in pulmonary function in normal subjects.
4. The children of smoking parents have an increased prevalence of reported respiratory symptoms, and have an increased frequency of bronchitis and pneumonia early in life.
5. The children of smoking parents appear to have measurable but small differences in tests of pulmonary function when compared with children of nonsmoking parents. The significance of this finding to the future development of lung disease is unknown.
6. Two studies have reported differences in measures of lung function in older populations between subjects chronically exposed to involuntary smoking and those who were not. This difference was not found in a younger and possibly less exposed population.

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7. The limited existing data yield conflicting results concerning the relationship between passive smoke exposure and pulmonary function changes in patients with asthma.

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CHAPTER 8. DEPOSITION AND TOXICITY OF TOBACCO SMOKE IN THE LUNG

CONTENTS

CIGARETTE SMOKE DEPOSITION IN THE LUNG

Introduction

Previous Reports of the Surgeon General on the health consequences of smoking have focused on characterizing and quantifying responses to the inhalation of cigarette smoke. Typically, dose is given in terms of packs per day or cumulative pack years. However, a more accurate description of dose would include how much smoke is inspired into the respiratory tract, how much is deposited and fails to exit with the expired air, and the fate of the deposited smoke.

A commonly held fallacy is that "living in New York is like smoking two packs per day." Is the amount of particles produced by smoking comparable to that encountered in urban air pollution? A person who smokes two packs of cigarettes per day with an average tar rating of 20 mg per cigarette would breathe in 800 mg of material per day, or 292 g of tar per year. A reasonable value for urban air would be 100 µg, or 0.1 mg per cubic meter. The average person breathes approximately 20,000 liters, or 20 cubic meters, of air per day. Thus, 2 mg of material per day, or 0.73 g of particulate per year, would be inspired. At the outset, it is evident that the amount of smoke entering the lungs is considerably greater than the amount of particulates from air pollution.

This chapter emphasizes the size and aerodynamic properties of smoke and relates them to the fraction of the inspired smoke that deposits in the lungs. Also considered is where the smoke deposits, and its possible fate is described.

The particulate phase of cigarette smoke, commonly known as tar, is inhaled as an aerosol into a smoker's respiratory tract. An aerosol is defined as a suspension of solid or liquid particles in a gas (Hinds 1982). In the case of cigarette smoke, the aerosol contains ambient air as well as the gases, liquids, and solids produced during tobacco combustion. The particulates include a wide variety of organic and metallic compounds, many of which are toxic to lung tissues. Hydrocarbons, aldehydes, ketones, organic acids, alcohols, nicotine, and phenols are among them. Metallic compounds such as radioactive lead and polonium are also present. The gas phase is also complex; in addition to the nitrogen and oxygen in the air, considerable amounts of carbon dioxide and carbon monoxide are present, and also significant amounts of cyanides, acrolein, nitrogen oxides, and ammonia. The precise quantitative composition of the tobacco smoke varies with many different factors, including the type of tobacco plant grown, the soil used to grow the plant, the method of curing the leaves, the temperature of combustion during smoking, and the composition and physical properties of the cigarette paper

and other additives. As the cigarette butt length decreases, many substances that have previously condensed on the remaining tobacco are revaporized. Generally, as butt length shortens, the smoke from the cigarette contains an increasing concentration of these substances. Most of these constituents in smoke are toxic to lung tissues. Their toxicity extends from impairment of mucociliary transport, critical for clearing particles from the lungs, to carcinogenic and cocarcinogenic activities (Wynder and Hoffmann 1979; Battista 1976). To understand where the numerous particulates in cigarette smoke deposit in the lungs and how they are removed is important for determining the pathologic effects of chronic cigarette smoking.

Characterization of an Aerosol

To predict the deposition patterns of any aerosol, such as cigarette smoke, it is necessary to know the size, shape, and density of the individual particles or droplets. Describing the distribution of particle diameters is essential. It is convenient to describe particle size as an aerodynamic diameter rather than as an actual particle size based on optical measurements, because the former is a better predictor of aerodynamic behavior (Hinds 1982). Aerodynamic diameter is defined as the diameter of a sphere of unit density that has the same settling velocity as the particle being measured. This may be expressed as a count median aerodynamic diameter (CMAD) and a mass median aerodynamic diameter (MMAD). These are, respectively, the diameters for which half of the number or mass of the particles are less than that diameter and half are more.

Characterization of Cigarette Smoke Aerosols

The particulates in cigarette smoke have been measured by several investigators using a variety of analytical devices. Because of different apparatus and different methods of smoke generation and dilution, results vary but are reasonably consistent. McCusker et al. (1983) used a device called the single particle aerodynamic relaxation time (SPART) analyzer to determine the size of particulates from several brands of cigarettes, with and without filters. The mass median aerodynamic diameter (MMAD) for all brands averaged approximately 0.46 μm; it was not markedly different when the filters were removed. These measurements showed that, even with a filter, billions of particles are present in an average 35 ml puff of cigarette smoke generated by an automatic smoking-machine. Particulate concentrations per ml ranged from 0.3×10^9 to 3.3×10^9, depending on whether the cigarettes were rated ultra-low, low, or medium in tar content. The reduced particulate concentration reported for low tar cigarettes results principally from filter

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efficiency and air dilution of the smoke. When the specially designed filters were removed or the vent holes were covered, as could be accomplished by the smoker's fingers, particulate concentrations per milliliter increased to levels comparable to that for higher tar content cigarettes.

Hinds (1978) compared the particulate size distribution in cigarette smoke using an aerosol centrifuge and a cascade impactor. Although these devices are based upon different physical principles, Hinds found that the results were comparable. The MMAD values ranged from 0.37 to 0.52 μm. Variations depended primarily upon the dilution of the smoke. The MMAD and concentration values reported by Hinds and coworkers (1983) were similar to those reported by Keith and Derrick (1960), who used a specially modified centrifuge, called a conifuge, to analyze cigarette smoke. Particulate analysis by a light scattering photometer yielded an MMAD of 0.29 μm and particulate concentrations of 3×10^{10} per ml (Okada and Matsunuma 1974). Carter and Hasegawa (1975) "fixed" cigarette particulates with methyl cyanoacrylate, a method that may produce artifacts, and measured a mean diameter of 0.48 μm from electron micrographs of the particulates. Earlier methods of measurement were based upon the collection of smoke particulates on various surfaces. Harris (1960) reported a range of 0.16 to 0.54 μm from a replica of cigarette smoke particulates that included a correction for droplet-spreading during sample preparation. Langer and Fisher (1956) found a median range of 0.6 μm, but made no correction for droplet-spreading during sample collection.

Time and concentration are important modifiers of tobacco smoke. Cigarette smoke aerosols contain volatile components, and evaporation gradually reduces particle diameters. It is also true that with the extremely high particle concentrations encountered in mainstream smoke, the aerosol can agglomerate rapidly because nearby particles collide with each other and coalesce. If smoke is cooled (reducing the vapor pressure of the volatile components) and diluted (reducing the probability of particle collisions) the particle size will be more stable. Thus, it is difficult to reliably measure the size and concentration of particles in cigarette smoke produced under realistic experimental conditions.

The size and concentration of the particulates are also affected by the decreasing length of a cigarette as it is smoked. McCusker et al. (1983) found the particulate concentration to be 67 percent greater in the last three puffs of a filtered cigarette than in the first three. Ishizu et al. (1978) also reported that particulate concentrations in unfiltered cigarettes increased and that the mean geometric diameter of the particles decreased with decreasing cigarette length. They attributed the former effect to the decreased filtration by the tobacco column and the latter effect to the shorter length traveled by the

particles to reach the butt end and, hence, the decreased time for particulate coagulation. In addition, their results illustrate that filters may trap the larger particles and generate more uniform aerosols; McCusker et al. (1983) noted no change in MMAD between the first and last three puffs of filtered cigarettes. Ishizu et al. (1978) also reported that larger puff volumes decreased the average particulate diameters. This can affect interpretation of experimental data in that standard cigarette smoking-machines draw 35 ml puff volumes, whereas Hinds et al. (1983) reported that 54 ml was the average puff volume measured in smoking subjects.

Particle size is a critical factor in determining what fraction of the particles that enter the respiratory tract will deposit there and fail to exit with the expired air, as well as where they will deposit. Submicrometric particles will deposit not only in small and large airways, but also in alveoli. Breathing pattern is also important (see review by Brain and Valberg 1979). Large tidal volumes will favor alveolar deposition. Higher inspiratory flows will promote deposition at bifurcations. Breath-holding is important, because the greater the elapsed time before the next expiration, the higher the fraction deposited (collection efficiency).

Individual anatomic differences may influence the amount and distribution of deposited particles. The cross-section of airways will influence the linear velocity of the inspired air. Increasing alveolar size decreases alveolar deposition.

Factors That Affect Particulate Deposition

A typical puff volume is approximately 30 to 70 ml. It is usually inspired with a volume of ambient air that is one to two times the normal tidal volume. Particle size not only can change in experimental equipment as described above, but also may change within the human respiratory tract.

After a volume of smoke is drawn into the mouth and upper respiratory tract of a smoker, it may be retained in that humidified air before deep inhalation. Here too, the particulates can change in size through coagulation or evaporation. They can also grow because of the particulates' affinity for water, termed hygroscopicity (Davies 1974; Hiller 1982b). Other aspects of each smoker's behavior may also influence dose. Most manufacturers achieve low tar yields by the use of ventilated cigarette holders; this causes the inhaled smoke to be diluted with air. However, 32 to 69 percent of interviewed smokers of "low" tar cigarettes reported that they blocked these filter preparations with their fingers or lips. This causes dramatic increases in the amount of tar and nicotine in a way not predicted by studies using smoking-machines (Kozlowski et al. 1980).

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Such individual differences in cigarette use as well as other strategies designed to increase the inhalation of tar and nicotine probably account for the poor correlation between the machine-determined nicotine yield of a cigarette and the concentration of nicotine or its metabolites in blood or urine (Russell et al. 1975, 1980; Sutton et al. 1982; Feyerabend et al. 1982; Benowitz et al. 1983). For example, Herning and coworkers (1981) demonstrated that when low nicotine cigarettes are used, most smokers compensate by increasing the puff volume. In addition, Tobin and Sackner (1982) reported that some subjects increase their puff volume by up to 70 percent after switching to low tar cigarettes. In some instances, this compensatory increase occurred during a single experimental session. In contrast, a few smokers may reduce smoke deposition in their lungs by retaining the smoke in their mouth for several seconds before inhaling it. Stupfel and Mordelet-Dambrine (1974) showed that if a smoker holds the smoke in his mouth for 2 seconds, 16 percent of the particulate matter is removed. Also, 60 percent of the water-soluble components of the gas phase are absorbed by the upper airways.

Chronic smoking also causes alterations in lung structure that affect deposition patterns. Sanchis et al. (1971) studied the deposition of an aerosol of radioactively labeled albumin inhaled by smokers and nonsmokers. They found less aerosol deposition in the alveolar region of smokers than of nonsmokers and suggested that the difference may be the result of alterations in the small airways produced by chronic smoking. Similar results were reported for hamsters exposed to cigarette smoke for 3 weeks prior to a single exposure of radioactively labeled cigarette smoke (Reznik and Samek 1980). More labeled smoke concentrate was found in the lungs of hamsters not previously exposed to cigarette smoke.

The rate and pattern of breathing can also affect the total dose of cigarette particulates deposited in the lungs. Dennis (1971) reported that exercise increased the percent deposition of two experimentally generated aerosols in human subjects. Increased deposition was also measured in exercising hamsters that inhaled a radiolabeled aerosol (Harbison and Brain 1983). These results are most relevant to those who smoke when ventilation is increased while working or shortly after a period of exercise.

Deposition of Cigarette Smoke Particulates

The factors discussed in the previous section illustrate that experimental measurements of the size and concentration of cigarette aerosols are insufficient for the prediction of deposition patterns. Cigarette smoke is a mutable aerosol, which complicates the collection of accurate and reproducible data regarding its particulate composition. In addition, alterations in respiratory

structure and respiratory rate can affect the deposition of particulates. These complexities stress the importance of actual measurement of the regional deposition of cigarette smoke particulates in human lungs. However, few data have been published on this important area, despite the prevalence of smoking and its impact on human health. Most of the available information on the deposition of cigarette smoke particulates is based upon theoretical or physical models of the lungs and measurements of differences in the concentration of aerosol between inhaled air and exhaled air.

A model to predict the percent deposition of particles based upon MMAD was presented by the Task Group on Lung Dynamics of the International Commission on Radiological Protection (1966). The respiratory tract was divided into three main regions: nasopharynx, trachea and bronchi, and alveoli. In conjunction with estimates of particulate clearance, deposition calculations were made for these regions at three different inhalation volumes. This model suggests that 30 to 40 percent of the particles within the size range present in cigarette smoke will deposit in the alveolar region and 5 to 10 percent will deposit in the tracheobronchial region. This model also emphasizes the impact of particle solubility on the total integrated dose over time. Brain and Valberg (1974) developed convenient nomograms and a computer program to demonstrate how particle solubility and particle size significantly affect the net amount of particulates retained in the lungs.

Aerosol deposition has also been studied in airway casts. Physical models of the upper airways of human lungs have been made by a double casting technique in order to study particulate deposition at several airway generations (Schlesinger and Lippmann 1972). Lungs obtained at autopsy were filled with wax or alloy. When these materials became solid, the tissue was removed and the casts were coated with silicon rubber or latex. The wax or alloy was then melted and removed, leaving a cast of the original airways. Different flow rates and particulate sizes were used to study deposition patterns. Schlesinger and Lippman (1978) reported a correlation between the deposition sites of test aerosols in the lung casts and the most common sites of origin of bronchogenic carcinoma in humans. Both occurred preferentially at bifurcations. Martonen and Lowe (1983) added an oropharyngeal compartment and a replica cast of the larynx to the tracheobronchial casts in order to better simulate air flow patterns in the upper respiratory tract. They used these models to evaluate the amount of cigarette smoke condensate deposited in the airways at different flow rates. More condensate was present at branching regions, especially at carinal ridges. Aerosol was also deposited preferentially along posterior airway walls.

Most experiments designed to determine aerosol deposition in human subjects measure differences in aerosol concentration before

and after inhalation. Hinds and associates (1983) measured the percent mass of inhaled tobacco smoke particulates that deposited in male and female smokers. A transducer placed in the filter of a smoked cigarette relayed information to an automatic smoking-machine to duplicate inhaled puff volume. This method was used to produce a more natural smoking pattern. Comparisons were then made between particulate mass concentrations in the machine-generated smoke and the amount of smoke actually exhaled by the smoker. With these measurements, a 57 percent deposition of particulate mass was seen in men. This was greater than the significant 40 percent collection efficiency measured in women ($p < 0.01$). No data regarding particulate size or deposition sites were reported. Hiller and coworkers (1982b) also measured the deposition fraction of an aerosol containing three different sizes of polystyrene latex spheres in nonsmoking humans. They measured a 10 percent deposition for 0.6 μm (MMAD) spheres, which is similar to the results of Davies et al. (1972) and Muir and Davies (1967) using 0.5 μm aerosols and of Heyder et al. (1973) using aerosols with a 0.2 to 1.0 μm range. The size ranges of these aerosols are comparable to those experimentally measured in cigarette smoke, as previously discussed. These percentages are lower than those observed by Hinds et al. (1983), probably reflecting differences in breathing patterns. The measurements of Hinds et al. (1983) were made with realistic breathing patterns used during smoking; the other investigators had used normal breathing patterns. Increased breath-holding following inspiration probably accounts for the enhanced collection efficiencies.

Particulate Retention in the Lung

The amount of particulates retained in the lung at different times following the inhalation of an aerosol such as cigarette smoke depends upon the balance between the amount that deposits in the respiratory tract and the efficiency of the lung clearance mechanisms in the airways and alveoli. Particles depositing in the airways are entrained in the mucus layer lining these passages. This layer is swept toward the mouth by the action of ciliated cells and eventually swallowed. Macrophages present in the airways may also phagocytose deposited particulates and are also carried toward the mouth by the mucociliary transport system. Particulates reaching the alveolar region—those that are usually smaller than several micrometers in size—are soon engulfed by alveolar macrophages. These cells gradually migrate toward the airways and exit the lung via the mucociliary escalator. Dissolution is also an important clearance mechanism for soluble particles. Clearance mechanisms are a dynamic component of normal lung function and operate to keep the lung sterile.

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Lung disease and cigarette smoking itself can affect particulate clearance and retention in smokers' lungs. Previous studies have shown that smokers have different aerosol deposition patterns and slower clearance rates than nonsmokers (Albert et al. 1969; Cohen et al. 1979; Sanchis et al. 1971). These alterations in clearance are, in part, caused by components in cigarette smoke that are ciliotoxic (Battista 1976) and impair phagocytosis by alveolar macrophages (Ferin et al. 1965). Clearance mechanisms in smokers may be further compromised by lung diseases, such as emphysema and fibrosis, and by exposure to air pollutants. Oxidants in photochemical smog, such as ozone and nitrogen oxides, are toxic to ciliated cells and macrophages (Bils and Christie 1980).

Measurements of retention of cigarette particulates in the lungs over time are difficult to estimate from data obtained with airway casts or from differences in the aerosol concentration of inhaled and exhaled smoke because these methods do not take clearance mechanisms into account. Unfortunately, few data are available regarding the actual retention and sites of deposition of cigarette smoke particulates in either humans or animals. The most accurate method is quantification of particulate deposits in individual pieces of tissue dissected from the lung. Impossible in living animals, this is a tedious procedure with animal lungs or human material obtained at surgery or autopsy and is especially difficult with large lungs. Little et al. (1965) examined lungs from humans at autopsy and suggested a correlation between the sites of bronchogenic carcinoma in the lungs of smokers with the deposition of polonium[210], a radioactive component of cigarette smoke. Resnik and Samek (1980) used a radioactive marker to study the retention of smoke in hamster lungs. They exposed hamsters to the smoke from cigarettes containing a labeled component in the tobacco and then measured the amount of radioactivity present in different lobes. They found that more radioactivity was present in the lung tissue of hamsters not previously exposed to unlabeled cigarette smoke. However, the clearance of the labeled component from the lungs was slower in the group previously exposed to smoke. There are problems with using animal models for smoke uptake. Most rodents are obligatory nose breathers, and significant fractions of the smoke may be taken up as it passes through the upper airways. Page et al. (1973) studied mice using radiolabeled cigarettes. They found that 50 percent of the deposited smoke was recovered from the nasal passages. About 30 percent was recovered from the esophagus, stomach, and other organs, and only 20 percent was present in the lungs. Exposing animals via a tracheostomy avoids this excessive and unnatural deposition in the nose, but it bypasses the mouth and larynx, which may remove some particles during smoking in man.

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Passive Smoking

Recently concern has increased regarding the health effects of cigarette smoke inhaled by nonsmokers, a phenomenon called passive smoking. The smoke is composed of that exhaled by the smoker and the sidestream smoke produced by the burning cigarette between inhalations. The concentration of respirable particulates in areas where there are smokers can range from 100 to 700 $\mu g/m^3$. This is up to 25 times higher than that found in nonsmoking areas (Repace and Lowrey 1980). Using mean deposition values of 11 and 70 percent for the passive smoker and the active smoker, respectively, from the data presented by Hiller et al. (1982), the deposition would be approximately 0.55 mg for a nonsmoker over an 8-hour day in a room with 500 $\mu g/m^3$ of smoke. In comparison, a smoker would deposit approximately 400 mg of tar in his or her lungs if he or she smoked two packs of cigarettes with an average tar rating of 20 mg per cigarette during the same time period. As has been discussed earlier, the rate and pattern of breathing can also affect the total dose of cigarette particulates deposited in the lungs.

Although the amount of smoke depositing in the lungs of nonsmokers during passive smoking is small compared to that encountered by the active smoker, large numbers of people are involved. In the United States in 1979, 36.9 percent of men and 28.2 percent of women were current smokers (USDHEW 1980).

Conclusions

Cigarette smoke is the most important cause of chronic obstructive lung disease. This significant response is matched by the significant dose of toxic particulates received by the respiratory tract of smokers. The particle size of cigarette smoke is so small that little protection is offered by the filtering capacity of the upper airways. Cigarette smoke penetrates deep into the lungs and reaches the small airways and alveoli. The fraction of the smoke deposited is high because most smokers employ some breath-holding following inhalation of a puff. Their attempt to enhance deposition of smoke is successful, resulting in increased lung burdens of toxic smoke products.